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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/589,381	08/15/2006	Annaliesa S. Anderson	21490YP	5673

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EXAMINER	
DEVI, SARVAMANGALA J N	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/589,381	ANDERSON ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/04/09*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5, 7 and 19-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5, 7, 19-24, 26-31, 33 and 34* is/are rejected.

7)☒ Claim(s) *25 and 32* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicant's Amendment

1) Acknowledgment is made of Applicant's amendment filed 12/04/09 in response to the non-final Office Action mailed 08/05/09.

Status of Claims

2) Claims 3, 5, 7, 24, 29 and 31 have been amended via the amendment filed 12/04/09.

Claim 6 has been canceled via the amendment filed 12/04/09.

New claims 33 and 34 have been added via the amendment filed 12/04/09.

Claims 1-5, 7 and 19-34 are pending and are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Moot

5) The rejection of claim 6 made in paragraph 10 of the Office Action mailed 08/05/09 under 35 U.S.C. § 101 as being directed to non-statutory subject matter, is moot in light of Applicants' cancellation of the claim.

6) The rejection of claim 6 made in paragraph 12 of the Office Action mailed 08/05/09 under 35 U.S.C. § 112, first paragraph, as containing inadequate written description, is moot in light of Applicants' cancellation of the claim.

7) The rejection of claim 6 made in paragraph 13 of the Office Action mailed 08/05/09 under 35 U.S.C. § 112, first paragraph, as containing new matter, is moot in light of Applicants' cancellation of the claim.

8) The rejection of claim 6 made in paragraph 14 of the Office Action mailed 08/05/09 under 35 U.S.C. § 112, first paragraph, as containing new matter, is moot in light of Applicants' cancellation of the claim.

9) The rejection of claim 6 made in paragraph 16 of the Office Action mailed 08/05/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

10) The rejection of claim 6 made in paragraph 18 of the Office Action mailed 08/05/09 under 35 U.S.C. § 102(e)(2) as being anticipated by Granoff *et al.* (US 7,534,444, filed 04/17/01, of record) ('444), is moot in light of Applicants' cancellation of the claim.

Rejection(s) Withdrawn

11) The rejection of claims 1, 5 and those dependent therefrom made in paragraph 10 of the Office Action mailed 08/05/09 under 35 U.S.C. § 101 as being directed to non-statutory subject matter, is withdrawn upon further consideration.

12) The rejection of claims 2, 3, 20, 24, 25 and 31 made in paragraph 13 of the Office Action mailed 08/05/09 under 35 U.S.C. § 112, first paragraph, as containing new matter, is withdrawn. Applicants point to second full paragraph of page 7 of the specification and submit that the specification therein describes a polypeptide at least 85% identical to SEQ ID NO: 1 containing up to 26 amino acid alterations from SEQ ID NO: 1; or differs from SEQ ID NO: 1 or SEQ ID NO: 2 by 0, 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, or 20 amino acid alterations.

13) The rejection of claim 3 made in paragraph 16(a) of the Office Action mailed 08/05/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

14) The rejection of claims 24 and 31 made in paragraph 16(b) of the Office Action mailed 08/05/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

15) The rejection of claim 5 made in paragraph 16(c) of the Office Action mailed 08/05/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of

Applicants' amendment to the claim.

16) The rejection of claim 5 made in paragraph 16(d) of the Office Action mailed 08/05/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

17) The rejection of claim 29 made in paragraph 16(e) of the Office Action mailed 08/05/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

18) The rejection of claims 4 and 7 made in paragraph 16(f) of the Office Action mailed 08/05/09 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

19) The rejection of claims 25 and 31 made in paragraph 12 of the Office Action mailed 08/05/09 under 35 U.S.C. § 112, first paragraph, as containing inadequate written description, is withdrawn in light of Applicants' amendment to the claims and/or the base claim.

Rejection(s) Maintained

20) The rejection of claims 1-3, 5, 7, 19-23 and 26-30 made in paragraph 12 of the Office Action mailed 08/05/09 under 35 U.S.C. § 112, first paragraph, as containing inadequate written description, is maintained for the reasons set forth therein and herein below.

New claims 33 and 34 are now added to this rejection.

Applicants submit the following arguments:

(a) The present application reasonably conveys to those skilled in the art that applicants were in possession of polypeptides having a substantially similar sequence to SEQ ID NO: 1 and which provide protective immunity against *S. aureus*. The reasonable conveyance is based on the high degree of structural relationship between the SEQ ID NO: 1 related polypeptides recited in the claims. (b) The data provided for SEQ ID NO: 3 illustrates that a polypeptide of SEQ ID NO: 1 is able to reproducibly provide for some protective immunity against a strain of S. *aureus*. SEQ ID NO: 3 is a His-tag version of SEQ ID NO: 1 (the present application at page 5, paragraphs 5-7). Figures 7A and 7B illustrate that more mice survive when immunized with a polypeptide vaccine (SEQ ID NO: 3) than with the adjuvant control. (c) Polypeptides having a high degree of structural similarity are expected to have similar properties. The rejection fails to take into

account the structurally similarity of the polypeptides recited in the claims. Instead, the rejection is based on the possibility that an alteration to a critical amino acid within the 260 amino acids of SEQ ID NO: 1 may impact a protein antibody interaction. (d) The rejection fails to provide any indication as to why a significant number of polypeptides within the scope of the claims would fail to provide protection. The possibility that some unknown alteration in an amino acid residue may impact a particular protein antibody interaction, does not necessarily equate to a polypeptide within the scope of claims not providing protective immunity. (e) SEQ ID NO: 1 is 260 amino acids in length and may contain more than one epitope providing a beneficial effect. SEQ ID NO: 1 is sufficiently representative of polypeptides described in the claims. The claims provide for varying high degrees of structural similarity ranging from SEQ ID NO: 1 to sequences with 1-15 amino acid alterations from SEQ ID NO: 1. The described high degree of structural relationship to SEQ ID NO: 1 provides more than a mere wish for obtaining a compound able to provide protective immunity. It provides a representative polypeptide and an expectation that polypeptides having a similar structure would have similar properties. Based on data provided in the application, the skilled artisan would expect a polypeptide of SEQ ID NO: 1 to provide protection against at least *S. aureus* COL and strains having a sai-1 sequence with a degree of sequence similarity to the *S. aureus* COL sequence. SEQ ID NO: 1 was obtained by making certain modifications to the naturally occurring COL sequence provided by SEQ ID NO: 7, and SEQ ID NO: 3 is a His-Tag version of SEQ ID NO: 1. (f) The patent office has failed to provide a rationale as why a significant number of polypeptides generally covered by the claims would not provide production against *S. aureus* COL.

Applicants' arguments have been carefully considered, but are not persuasive. Contrary to Applicants' allegation, the Office has set forth more than sufficient rationale and has established a clear lack of written description. The recited amino acid alterations are not limited to amino acid additions at the amino or the carboxyl terminus of SEQ ID NO: 1, but include alterations, substitutions and deletions within SEQ IDNO: 1. The Office has previously established that polypeptides having any degree of structural similarity are not necessarily expected to have similar properties absent a concrete structure-function correlation. The lack of functional predictability in the art was previously established via documentation of the teachings from Skolnick *et al. Trends in Biotechnology* 18: 34-39, 2000; Colman PM. *Research Immunol.*

145: 33-36, 1994; and Houghten *et al*. New Approaches to Immunization, *Vaccines86*, Cold Spring Harbor Laboratory, pages 21-25, 1986, all of record. Applicants have failed to advance any arguments to address the art-recognized unpredictability documented via the teachings of multiple references. Without addressing the teachings of these references cited as a part of the rejection and without establishing a structure-function correlation for the polypeptide variants encompassed within the scope of the claims, one cannot speculate that polypeptides having a high degree of structural similarity are expected to have similar properties. With regard to Applicants' argument that the rejection is based on the possibility that an alteration to a critical amino acid within the 260 amino acids of SEQ ID NO: 1 may impact a protein antibody interaction, the following should be noted. As set forth previously, for an altered polypeptide to be protective, it has to minimally bind immunospecifically with a protective antibody specific to the native polypeptide. Therefore, interaction between a protein and its specific antibody is very relevant for immunospecific protection. As set forth previously, the state of the art documents that a change of even a single amino acid residue can alter the folding of a polypeptide such that the antibody-binding region no longer recognizes the polypeptide. See right column on page 33 of Colman PM. *Research Immunol*. 145: 33-36, 1994, of record. Without such immunospecific recognition, there cannot be any immunoprotection. It is recognized in the art that even a very conservative substitution may abolish binding. See first full paragraph on page 35 of Colman. Colman further taught that binding interactions could be considered less tolerant because the changes involved occur in what might be called the active site. See third full paragraph on page 35 of Colman. In an unpredictable art, adequate written description of a genus embracing widely variant species cannot be achieved by disclosing one species within the genus, but through sufficient description of a representative number of species within the claimed genus. In the instant case, as set forth previously, the precise structure of a representative number of variant species of SEQ ID NO: 1 or the variant species altered within SEQ ID NO: 1 as claimed, has not been correlated with the requisite function, i.e., induction of protective immunity against any strain of *S. aureus*. SEQ ID NO: 3 is a His-tagged SEQ ID NO: 1 and is representative of a polypeptide consisting of SEQ ID NO: 1 and additional amino acids at one of its terminus, but is not representative of the claimed polypeptide variant genus having amino acid alteration(s) within SEQ ID NO: 1 or non-identity with SEQ ID NO: 1 having the ability to provide protective

immunity against of *S. aureus*. The protein-antibody interaction is minimally needed for immunospecific protection since the antibodies induced by the polypeptide variants are required to first recognize the native polypeptide on pathogenic *S. aureus* cells and then confer protection against pathogenic *S. aureus*. Without a structure-function correlation and without the identification of one or more domains, or contiguous or discontiguous epitopes, linear or conformational epitopes responsible for providing protective immunity against a homologous or heterologous *S. sureus*, one of skill in the art would not recognize that inventors had possession of the full scope of the invention as claimed at the time of the invention. The specification fails to teach the structure or precise relevant identifying characteristics of a representative number of such altered polypeptide species sufficient to allow one skilled in the art to determine that inventors had possession of the invention as claimed. Applicants have not described which domains or active regions of the recited polypeptide immunogen variants are correlated with the required capacity to provide such protective immunity. Applicants have not described which of SEQ ID NO: 1's amino acids can be varied such that the polypeptide immunogen variant still maintains the capacity to provide such broad protective immunity. Without a convincing correlation between structure and function, the claims do little more than define the claimed invention by function. That is not sufficient to satisfy the written description requirement. *Ex parte Kubin*, 83 USPQ2d 1410 (Bd. Pat. Appl. & Int. 2007) citing *Eli Lilly*, 119 F.3d at 1568, 43 USPQ at 1406 ('definition by function ….. does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is'). Furthermore, the new claims 33 and 34 include the limitation: 'a polypeptide immunogen consists of 'an' amino acid sequence of SEQ ID NO: 1 ……, wherein said polypeptide immunogen provides protective immunity against a *S. aureus*'. The limitation 'a polypeptide immunogen consists of 'an' amino acid sequence of SEQ ID NO: 1 … wherein said polypeptide immunogen provides protective immunity against a *S. aureus*' encompasses a polypeptide consisting of a short fragment from any region from within SEQ ID NO: 1 wherein the fragment has to provide immunity against a *S. aureus*. However, Applicants have not described a representative number of such fragment species of SEQ ID NO: 1 and have not correlated the precise structure of such fragments with the requisite function, i.e., induction of protective immunity against any strain of *S. aureus*. The instant claims do not meet the written description provision of 35 U.S.C. § 112, first paragraph. The rejection stands.

21) The rejection of claim 5 and those dependent therefrom made in paragraph 14 of the Office Action mailed 08/05/09 under 35 U.S.C. § 112, first paragraph, as containing new matter, is maintained for the reasons set forth therein and herein below.

New claims 33 and 34, dependent from claim 5, are now added to this rejection.

Applicants submit that the objected to phrase "wherein said sai-1 region is present on a sequence found in *a S. aureus* sequence" is directed to a naturally occurring *S. aureus* sai-1 polypeptide region. Applicants state that claim 5 was amended to more particularly reference the sia-region as a polypeptide, support for which is found at second paragraph on pages 3 and 6 [Emphasis added]:

> Reference to "additional region or moiety" indicates a region or moiety different from a **sai-1 region**. The additional region or moiety can be, for example, an additional polypeptide region or a non-peptide region.
>
> Different sai-1 sequences may be present in different strains of *S. aureus*. Two examples of **sai-1 sequences are provided by SEQ ID NO: 7 and 8**. Other naturally occurring sai-1 sequences can be identified based on the presence of a high degree of sequence similarity or contiguous amino acids compared to a known sai-1 sequence. Contiguous amino acids provide characteristic tags. In different embodiments, a naturally occurring **sai-1 sequence** is a sequence found in a *Staphylococcus,* preferably *S. aureus,* having at least 20, at least 30, or at least 50 contiguous amino acids as in SEQ ID NO: 1; and/or having at least 85% sequence similarity or identity with SEQ ID NO: 1.

Applicants further assert that SEQ ID NOs: 7 and 8 are polypeptides.

Applicants' arguments have been carefully considered, but are not persuasive. Claim 5, as amended, includes the limitations: 'different from a sia-1 polypeptide region … having at least one of the properties …. wherein said sia-1 polypeptide **region** is present on a *S. aureus* polypeptide sequence having at least 30 contiguous amino acids as provided in SEQ ID NO: 1'. What are described at page 6 of the specification are sia-1 polypeptide *sequences,* SEQ ID NO: 7 and 8, or a naturally occurring sia-1 *sequence found in S. aureus* having at least 30 contiguous amino acids as in SEQ ID NO: 1. The described sia-1 sequences *found in S. aureus* having at least 30 contiguous amino acids as in SEQ ID NO: 1 are full length sequences. What is recited in the claim is 'a region different from a sia-1 polypeptide region' having at least one of the three specifically recited properties, for which there is no descriptive support in the as-filed specification. The rejection stands.

22) The rejection of claims 1, 5, 7, 19, 21-23 and 26-30 made in paragraph 18 of the Office Action mailed 08/05/09 under 35 U.S.C. § 102(e)(2) as being anticipated by Granoff *et al.* (US

7,534,444, filed 04/17/01) ('444), is maintained for the reasons set forth therein and herein below.

New claims 33 and 34, dependent from claim 5, are now added to this rejection.

Applicants contend that the sequences referenced in Granoff *et al.* are not SEQ ID NO: 1, and differ from SEQ ID NO: 1 by more the number of amino acids differences mentioned in the rejected claims. Applicants state that the office action appears to point to only a three amino acid overlap.

Applicants' arguments have been carefully considered, but are not persuasive. The limitation 'an amino acid sequence of SEQ ID NO: 1' in instant claims 1, 5, 21-23, 26 and 28-30 has no size or length limit or a structure limit. The QTP sequence taught by Granoff *et al.* qualifies as 'an' amino acid sequence of SEQ ID NO: 1 as recited in these claims and meets the claim limitation of a polypeptide immunogen 'consisting of an amino acid sequence of SEQ ID NO: 1'. As set forth previously, Granoff *et al.* ('444) disclosed an isolated and purified polypeptide consisting of the amino acid sequence, QTP, and a polypeptide consisting of QTP and an additional region or moiety sequence, FVQ or VHS covalently joined to said QTP sequence at its amino or carboxy terminus respectively. A composition comprising an immunologically effective amount of the same in a pharmaceutically acceptable carrier and an adjuvant is taught. See Figures 4A and 4B; lines 23-61 in column 5; lines 10-13 of column 4; lines 34-40 in column 7; last paragraph in columns 22 and 24; first paragraph in column 23; and paragraph bridging columns 15 and 16. The prior art polypeptide immunogen binds to a specific bactericidal protective antibody and therefore contains a protective epitope. The prior art sequence polypeptide consisting of the QTP sequence necessarily constitutes 'an amino acid sequence of SEQ ID NO: 1' since it forms a fragment of the instantly recited SEQ ID NO: 1 that is located at its 210-212 positions. The FVQ region or moiety present at the amino terminus or the QTP sequence or the VHA region or moiety present at the carboxyl terminus of the QTP sequence is different from the sai-1 polypeptide region and is expected to facilitate polypeptide stability. The Office's position that the prior art polypeptide is the same as the instantly claimed polypeptide or immunogen is based on the fact that the prior art QTP sequence is structurally identical to 'an amino acid sequence of SEQ ID NO: 1'. The ability to provide protective immunity against *S. aureus* or *S. aureus* COL is viewed as an inherent property inseparable from the structurally

identical prior art sequence and the prior art composition comprising the sequence. The rejection stands.

New Rejection(s) Necessitated by Applicants' Amendment

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

23) The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude one or more claims particularly pointing out and distinctly claiming the subject matter which the Applicant regards as his/her invention.

24) Claims 3, 4, 24, 31, 33 and 34 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite, for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 33 is incorrect in the limitation: differs from SEQ ID NO: 1 'by with'.

(b) In claims 3, 24 and 31, for proper antecedence and for consistency with the claim language used in line 7 of claim 5, it is suggested that Applicants replace the limitation 'amino terminus' with the limitation --the amino terminus--.

(c) Claim 3, as amended, is indefinite in the limitation: 'polypeptide immunogen of claim 1 …. consists of … amino acids 3-260 of SED ID NO: 1 and up to 15 additional amino acids at the carboxyl or amino terminus'. Claim 3 depends from claim 1, wherein the polypeptide immunogen consists of a sequence that differs from SEQ ID NO: 1 by *up to 15 amino acid alterations*. The term 'amino acid alterations' is defined in the specification as including amino acid additions. The above-identified limitation in claim 3 includes deletion of amino acids 1 and 2 of SEQ ID NO: 1 (i.e., 2 amino acid alterations) plus the addition of 14 or 15 amino acids (i.e., 14 or 15 amino acid alterations) at the carboxyl or the amino terminus of SEQ ID NO: 1 thus totaling more than 15 amino acid alterations and therefore is improperly broadening relative to the polypeptide immunogen of the base claim 1 that is required to consist of a sequence differing from SEQ ID NO: 1 by *up to 15 amino acid alterations*.

(d) Analogous rejection and criticism apply to claims 24 and 31 with regard to the limitation: 'polypeptide immunogen of claim 1 …. consists of … amino acids 3-260 of SED ID NO: 1 and up to 15 additional amino acids at the carboxyl or amino terminus'.

(e) Claims 4 and 34, which depend from claims 3 and 33 respectively, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Relevant Art

25) The prior art made of record and not relied upon in any of the rejections is considered pertinent to Applicants' disclosure:

- With regard to the structure-function relationship of an encoded amino acid sequence in general, Rudinger *et al.* (*In*: *Peptide Hormones*. (Ed) JA Parsons, University Park Press, pages 1-7, June 1976) taught that 'the significance of particular amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study'. See page 6. Rudinger *et al.* further taught that 'it is impossible to attach a unique significance to any residue in a sequence' and that a 'given amino acid will not by any means have the same significance in different peptide sequences, or even in different positions of the same sequence. See page 3.

- The state of the art reflects unpredictability as to which amino acids in a specific protein can be varied, i.e., replaced or added, without adversely affecting the functional properties of that specific protein. In other words, the retention of the immunospecificity following one or more amino acid substitutions, including conservative amino acid substitutions within a bacterial polypeptide is not predictable. For instance:

  (A) McGuinnes *et al.* (*Mol. Microbiol.* 7: 505-514, 1993, of record) taught that "[a] single amino acid change within an epitope, or an amino acid deletion *outside* an epitope, were both associated with loss of subtype specificity resulting from a change in the predicted conformation at the apex of the loop structure" in case of a meningococcal polypeptide. See abstract.

  (B) Similarly, (B) McGuinnes *et al.* (*Lancet* 337: 514-517, March 1991, of record) taught that a point mutation generating a single amino acid change in a P1.16-specific epitope in the VR2 region of the *porA* gene of a strain of *Neisseria meningitidis* of subtype P1.7,16 resulted in "striking changes in the structural and immunological properties of the class 1 protein" of this isolate. See abstract and page 514.

- US 2006-0177462 A1 documents the functional unpredictability associated with variants of staphylococcal polypeptides. For example, a purified polypeptide immunogen consisting of SEQ ID NO: 1, which is a truncated full length ORF0657n polypeptide (SEQ ID

NO. 2) of *S. aureus* COL, is shown to be protective against a strain of *S. aureus*. See Figure 1A. However, a polypeptide variant consisting of an amino acid sequence that is 90.58% identical to said SEQ ID NO: 1, depicted as fragment 2 in Figure 1A via one of the open rectangles, was found **not** to be protective. See paragraph [0032]. This is indicative of unpredictability in obtaining a polypeptide species that is about 10% non-identical in structure to SEQ ID NO: 1 and that remains protective against *S. aureus* infection. Furthermore, paragraph [0047] states that a fragment of SEQ ID NO: 2 consisting of amino acids 82-486 or amino acids 42-196 was **not** protective. This documented non-protection by the fragments of SEQ ID NO: 2 or 1 consisting of amino acids 82-486 or 42-196 appears to indicate the absence of one or more protective epitopes in these regions. Thus, the unmodified SEQ ID NO: 1 when merely split into a fragment of amino acids 82-486, or amino acids 42-196, looses its protective capacity, indicating the criticality of retaining all the amino acid residues of SEQ ID NO: 1 intact within the claimed fragment/variant in order to retain the requisite function of providing protective immunity against *S. aureus*. Thus, there is a lack of predictability as to whether polypeptide variants having up to 10% non-identity to SEQ ID NO: 1 anywhere along SEQ ID NO: 1 would remain immunospecific to *S. aureus* and provide protective immunity against *S. aureus* in a human or a non-human host.

- It is well established in the art that immunogenicity/antigenicity does not correlate with protection from infection. Chandrashekar *et al* (US Patent 6,248,329) taught '... it is well understood that the ability of an antigen to stimulate antibody production does not necessarily correlate with the ability of the antigen to stimulate an immune response capable of protecting an animal from infection..'. See column 1, lines 35-42.

- Foster *et al*. (US 2003/0186275 A1) disclosed a polypeptide immunogen of *S. aureus* consisting of an 106 amino acid-long sequence of the instantly recited SEQ ID NO: 1. See the SEQ ID NO: 14 on page 23. A vaccine composition against *Staphylococcus* spp. or against *S. aureus* or *S. epidermidis* comprising the protein in a carrier and/or an adjuvant for immunizing an animal or human is taught. See paragraphs [0055] to [0064]; the 106 amino acid-long *S. aureus* protein consisting of the amino acid sequence of SEQ ID NO: 14 on page 23; claims 18, 17 and 24-32.

Remarks

26) Claims 1-5, 7, 19-24, 26-31, 33 and 34 stand rejected.

Claims 25 and 32 are objected to as being dependent from a rejected claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

A polypeptide immunogen consisting of SEQ ID NO: 1, with or without up to 15 amino acids at its carboxyl or amino terminus is free of prior art currently of record.

In claims 23 and 31, it is suggested that Applicants replace the limitation 'by up to 1' with the limitation --by 1--.

27) Applicants' amendment necessitated the new ground(s) of rejection presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

28) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. The Fax number for submission of amendments, responses and/or papers is (571) 273-8300, which receives transmissions 24 hours a day and 7 days a week.

29) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would

like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (in USA or CANADA) or 571-272-1000.

30) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Robert Mondesi, can be reached on (571) 272-0956.

/S. Devi/
Primary Examiner
AU 1645

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